Amendment to the Claims:

1.–21. (Cancelled)

22. (Previously presented) A method of screening for a candidate substance which inhibits the phosphorylation of a tau protein by casein kinase 1 (CK1), the method comprising:

(a)

i) said candidate substance;

ii) a tau protein comprising the amino acid sequence of SEQ ID NO:2, or a tau variant comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:2, said tau protein or tau variant including one or more phosphorylation sites S46, T50, S113, S131, T149, T169, S184, S208, S210, T212, S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, S412, S413, T414, S416, S433 and S435, said phosphorylation sites corresponding to the amino acid sequence of SEQ ID NO:2;

iii) a CK1 polypeptide comprising the amino acid sequence of SEQ ID NO: 1, or a CK1 variant comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1, wherein said CK1 polypeptide or CK1 variant phosphorylates the tau protein or the tau variant of ii) at one or more sites selected from the group consisting of (S46/T50), S113, S131, T149, T169, S184, S208, (S210/T212), S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, (S412/S413/T414), S416, S433 and S435 corresponding to the amino acid sequence of SEQ ID NO:2;

(b) determining whether, and optionally the extent to which the candidate substance of i) inhibits phosphorylation of the tau protein or tau variant of ii) by the CK1 polypeptide or CK1 variant of iii) at one or more sites selected from the group consisting of (S46/T50), S113, S131, T149, T169, S184, S208, (S210/T212), S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, (S412/S413/T414), S416, S433 or S435 corresponding to the amino acid sequence of SEQ ID NO:2; and

(c) selecting the candidate substance that inhibits phosphorylation of said tau protein or tau variant at one or more phosphorylation sites.

23-25. (Cancelled)

26. (Previously presented) The method of claim 22, wherein the tau protein is paired helical filament tau.

27. (Previously presented) The method of claim 22, wherein the tau protein is a fragment of SEQ ID NO: 2 having one or more said phosphorylation sites.

28-30. (Cancelled)

31. (Withdrawn) The method of claim 22, wherein the sites of the tau protein are selected from S262 and/or S356.

32. (Previously presented) The method of claim 22, wherein the sites of the tau protein are one or more sites selected from the group consisting of S113, S258, S289, S416, S433 and S435.

33. (Withdrawn) The method of claim 22, wherein the method comprises determining the effect of contacting the candidate substance(s) with a combination of kinases, simultaneously or sequentially applied to the candidate substances and casein kinase 1.

34. (Withdrawn) The method of claim 33, wherein the combination of kinases comprises casein kinase 1 (CK1) in combination with one or more of casein kinase 2 (CK2), protein kinase A (PKA), glycogen synthase kinase 3α (GSK-3α) or glycogen synthase kinase 3β (GSK-3β).

35. (Withdrawn) The method of claim 33, wherein the combination of kinases comprises casein kinase 1 (CK1) in combination with PKA and GSK-3β.

36. (Previously presented) The method of claim 22, wherein the method further comprises determining in step (b) whether, and optionally the extent to which, the candidate substance inhibits the phosphorylation of another substrate by the casein kinase 1.

37. (Cancelled)

38. (Previously presented) The method of claim 36, wherein the method further comprises confirming whether a candidate substance selected in an initial screen has the property of inhibiting the phosphorylation of the tau protein under conditions in which the casein kinase 1 is capable of phosphorylating the site(s) of the tau protein in the absence of the candidate substance.

39. (Previously presented) The method of claim 22, wherein the step of determining the presence, absence or extent of phosphorylation at one or more sites of the tau protein employs mass spectroscopy or a site specific recognition agent which is capable of distinguishing between a phosphorylated and a non-phosphorylated site.

40. (Withdrawn) The method of claim 39, wherein the site specific recognition agent is a monoclonal antibody.

41. (Previously presented) The method of claim 22, wherein the screening is carried out in a multiplex assay employing a solid phase on which a plurality of substrates are immobilised.

42. (Original) The method of claim 41, wherein the substrates correspond to phosphorylation sites of tau protein.

43. (Withdrawn) The method of claim 22, comprising the further step of optimising the structure of the selected candidate substance.

44. (Withdrawn) The method of claim 22 which comprises at least one of the further steps of manufacturing the selected candidate substance and formulating the selected candidate substance in a pharmaceutical composition.

45. (Withdrawn) A method of preparing a pharmaceutical composition or medicament, the

method comprising:

(i) identifying a casein kinase 1 inhibitor according to claim 22;

(ii) optimising the structure of the casein kinase 1 inhibitor; and

(iii) preparing the pharmaceutical composition or medicament containing the optimised casein kinase 1 inhibitor.

46. (Withdrawn) A substance obtained by the method of claim 22.

47.– 52. (Cancelled)

53. (Withdrawn) A method for the treatment of a tauopathy in a patient in need of said treatment, said method comprising administering to said patient a substance obtainable by the method of claim 22.

54. (Withdrawn) The method of claim 53 wherein the tauopathy is Alzheimer's disease, frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), progressive supranuclear palsy (PSP), Pick's disease, corticobasal degeneration, multisystem atrophy (MSA), neurobasal degeneration with iron accumulation, type 1 (Hallervorden-Spatz), argyrophilic grain dementia, Down's syndrome, diffuse neurofibrillary tangles with calcification, dementia pugilistica, Gerstmann-Sträussler-Scheinker disease, myotonic dystrophy, Niemann-Pick disease type C, progressive subcortical gliosis, prion protein cerebral amyloid angiopathy, tangle only dementia, postencephalitic parkinsonism, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, amyotrophic lateral sclerosis/parkinsonism-dementia complex, non-Guamanian motor neuron disease with neurofibrillary tangles/dementia, and Parkinson's disease.

55. (Currently amended) The method of claim 22, said phosphorylation site(s) being at least one selected from the group consisting of S113, S237, S238, S258, S289, S412, S413, T414, S416, S433, and S435.